



1614

# EXPRESS MAIL CERTIFICATE

Express Mail" Label No. : EV 032 196 842 US

Date of Deposit : July 30, 2002

Serial No. : 10/091,759

Applicant(s) : Adnan M. M. Mjalli et al.

Filing Date : March 5, 2002

Title: : CARBOXAMIDE DERIVATIVES AS  
THERAPEUTIC AGENTS

Examiner : Unassigned

Group Art Unit : 1614

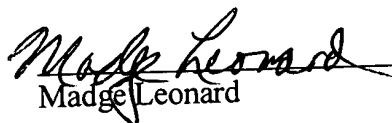
Type of Document(s) : Transmittal Form  
Information Disclosure Statement (in duplicate)  
PTO/SB/08A  
References: 68 References  
Return Postcard

RECEIVED

AUG 05 2002

TECH CENTER 1600/2800

I hereby certify that the documents identified above are being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and are addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

 (signature)  
Madge Leonard

Please type a plus sign (+) inside this box →

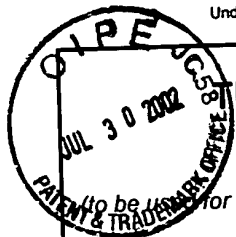


EV 032 196 842 US PTO/SB/21 (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number



# TRANSMITTAL FORM

Do not be used for all correspondence after initial filing)

Total Number of Items in This Submission (including Transmittal Form)

73

Application Number

10/091,759

Filing Date

March 5, 2002

First Named Inventor

Adnan M. M. Mjualli

Group Art Unit

1614

Examiner Name

Unassigned

Attorney Docket Number

41305-271123 (2001-21)

## ENCLOSURES (check all that apply)

☐ Fee Transmittal Form

☐ Fee Attached

☐ Amendment / Response

☐ After Final

☐ Affidavits/declaration(s)

☐ Extension of Time Request

☐ Express Abandonment Request

☒ Information Disclosure Statement (in duplicate)

☐ Certified Copy of Priority Document(s)

☐ Response to Missing Parts/ Incomplete Application

☐ Response to Missing Parts under 37 CFR 1.52 or 1.53

☐ Assignment Papers (for an Application)

☐ Drawing(s)

☐ Licensing-related Papers

☐ Petition

☐ Petition to Convert to a Provisional Application

☐ Power of Attorney, Revocation Change of Correspondence Address

☐ Terminal Disclaimer

☐ Request for Refund

☐ CD, Number of CD(s) \_\_\_\_\_

☐ After Allowance Communication to Group

☐ Appeal Communication to Board of Appeals and Interferences

☐ Appeal Communication to Group (Appeal Notice, Brief, Reply Brief)

☐ Proprietary Information

☐ Status Letter

☒ Other Enclosure(s) (please identify below):  
Express Mail Certificate -  
EV 032 196 842 US  
PTO/SB/08A (4 pages)  
References - 68  
Return Postcard

Remarks

## SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm or Individual name

Cynthia B. Rothschild, Esq.  
Reg. No. 47,040

Signature

*Cynthia B. Rothschild*

Date

7/30/02

## CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service's first class mail in an envelope

addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231 on this date:

Typed or printed name

SENT VIA EXPRESS MAIL

Signature

Date

Burden Hour Statement: This form is estimated to take 0.2 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

41305-271123

WINLIB01:957017.1

RECEIVED

AUG 05 2002

TECH CENTER 1600/2900

TTP2001-21

EV 032 196 842 US  
PATENT

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of

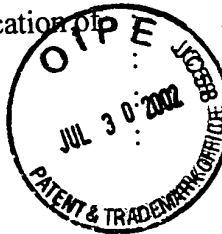
Serial No.

Filing Date

Title

Examiner

Group Art Unit



Adnan M. M. Mjalli et al.

10/091,759

March 5, 2002

CARBOXAMIDE DERIVATIVES AS  
THERAPEUTIC AGENTS

Unassigned

1614

Assistant Commissioner of Patents  
Washington, DC 20231

**RECEIVED**

AUG 05 2002

TECH CENTER 1600/2900

Sir:

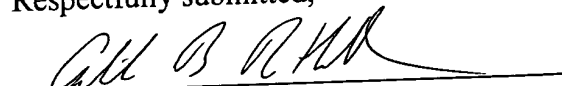
**INFORMATION DISCLOSURE STATEMENT**

Pursuant to 37 C.F.R. §§ 1.56, 1.97 and 1.98, the attention of the Patent and Trademark Office is hereby directed to the references listed on the attached Form PTO/SB/08A. A copy of each of the references listed on the attached form is submitted herewith.

It is respectfully requested that the references listed on the attached form be expressly considered by the Examiner and be made of record in the application and appear among the "References Cited" on any patent to issue therefrom.

This Information Disclosure Statement is being submitted prior to the mailing of a first action on the merits in the present application. Accordingly, it is believed that no fees are due for consideration of this Information Disclosure Statement. However, should any fees be due, the Assistant Commissioner is authorized to charge such fees to Deposit Account 16-1435. A duplicate of this sheet is attached for that purpose.

Respectfully submitted,

  
Cynthia B. Rothschild, Reg. No. 47,040

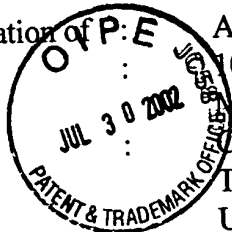
Date: 7/30/02

KILPATRICK STOCKTON LLP  
1001 West Fourth Street  
Winston-Salem, North Carolina 27101-2400  
(336) 747-7541 Phone  
(336) 607-7500 Facsimile  
Attorney Docket No.: 41305-271123

41305-271123 WINLIB01:957000.1

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of Adnan M. M. Mjalli et al.  
Serial No. : 10/091,759  
Filing Date : March 5, 2002  
Title : CARBOXAMIDE DERIVATIVES AS  
THERAPEUTIC AGENTS  
Examiner : Unassigned  
Group Art Unit : 1614



Assistant Commissioner of Patents  
Washington, DC 20231

RECEIVED

AUG 05 2002

TECH CENTER 1600/2900

Sir:

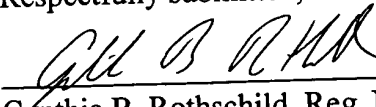
INFORMATION DISCLOSURE STATEMENT

Pursuant to 37 C.F.R. §§ 1.56, 1.97 and 1.98, the attention of the Patent and Trademark Office is hereby directed to the references listed on the attached Form PTO/SB/08A. A copy of each of the references listed on the attached form is submitted herewith.

It is respectfully requested that the references listed on the attached form be expressly considered by the Examiner and be made of record in the application and appear among the "References Cited" on any patent to issue therefrom.

This Information Disclosure Statement is being submitted prior to the mailing of a first action on the merits in the present application. Accordingly, it is believed that no fees are due for consideration of this Information Disclosure Statement. However, should any fees be due, the Assistant Commissioner is authorized to charge such fees to Deposit Account 16-1435. A duplicate of this sheet is attached for that purpose.

Respectfully submitted,

Date: 7/30/02  
Cynthia B. Rothschild, Reg. No. 47,040

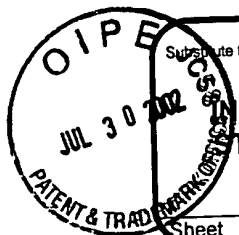
KILPATRICK STOCKTON LLP  
1001 West Fourth Street  
Winston-Salem, North Carolina 27101-2400  
(336) 747-7541 Phone  
(336) 607-7500 Facsimile  
Attorney Docket No.: 41305-271123

Please type a plus sign (+) inside this box → +

PTO/SB/O&A (08-00)

Approved for use through 10/31/2002. OMB 0651-0031  
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number



Substitute for form 1449APTO

## INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 1 of 4

Complete if Known

Application Number	10/091,759
Filing Date	March 5, 2002
First Named Inventor	Adnan M.M. Mjalli
Group Art Unit	1614
Examiner Name	Unassigned
Attorney Docket Number	41305-271123 (2002)
Express Mail Certificate	EV 032 196 842 US

RECEIVED

AUG 05 2002

TECH CENTER 600/2900

### U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication Cited Document MM-DD-YYYY	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code <sup>2</sup> (if known)			
	1	4,166,452		Generales, Jr.	09-04-79	
	2	4,265,874		Bonsen, et al.	05-05-81	
	3	4,356,108		Schwab, et al.	10-26-82	
	4	4,873,313		Crawford, et al.	10-10-89	
	5	5,202,424		Vlassara, et al.	04-13-93	
	6	5,585,344		Vlassara, et al.	12-17-96	
	7	5,688,653		Ulrich, et al.	11-18-97	
	8	5,864,018		Morser, et al.	01-26-99	
	9	5,939,526		Gaugler, et al.	08-17-99	
	10	6,100,098		Newkirk	08-08-00	

### FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>3</sup>
		Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>2</sup> (if known)				
	11	WO	00/20458		The Trustees of Columbia University in NYC	04-13-00		✓
	12	WO	00/20621		The Trustees of Columbia University in NYC	04-13-00		✓
	13	WO	97/26913		The Trustees of Columbia University in NYC	07-31-97		✓
	14	WO	97/39121		Schering Aktiengesellschaft	10-23-97		✓
	15	WO	9739125		Schering Aktiengesellschaft	10-23-97		✓
	16	WO	98/22138		The Trustees of Columbia University in NYC	05-28-98		✓
	17	WO	99/07402		The Trustees of Columbia University in NYC	02-18-99		✓
	18	WO	99/18987		The Trustees of Columbia University in NYC	04-22-99		✓
	19	WO	99/54485		The Trustees of Columbia University in NYC	10-28-99		✓
	20	WO	95/09838		Merrell Dow Pharmaceuticals Inc.	04-13-95		✓
	21	WO	95/35279		Merrell Pharmaceuticals Inc.	12-28-95		✓
	22	WO	97/22618		Vertex Pharma- ceuticals Incorporated	06-26-97		✓
	23	WO	96/32385		Hoechst Marion Roussel Inc.	10-17-96		✓
	24	WO	99/50230		Vertex Pharma- ceuticals Incorporated	10-07-99		✓

Please type a plus sign (+) inside this box → +

PTO/SB/08A (08-00)

Approved for use through 10/31/2002. OMB 0651-0031  
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449APTO

# **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet 2 of 4

Complete if Known

**RECEIVED**

Application Number 10/091,759  
Filing Date March 5, 2002  
First Named Inventor Adnan M.M. Mjalli  
Group Art Unit 1614  
Examiner Name Unassigned  
Attorney Docket Number 41305-271123 (2002)  
Express Mail Certificate EV 032 196 842 US

AUG 05 2002

TECH CENTER 1600/2900

25	GB	2 005 674	Carlo Erba S.p.A.	04-25-79	✓
26	WO	98/33492	Fox Chase Cancer Center	08-06-98	✓
27	WO	99/25690	University of Kansas Medical Center	05-27-99	✓
28	WO	01/12598	The Trustees of Columbia University in New York City, NY	02-22-01	✓

## **OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
	29	Albercio, F. & Carpino, L.A., "Coupling Reagents and Activation" <i>Methods in Enzymology</i> 289:104-126, Academic Press, San Diego (1997)	✓
	30	Barton, J.W., "In Protection of N-H Bonds and NR <sub>3</sub> " <i>Protective Groups in Organic Chemistry</i> , J.F.W. McOmie, ED., Plenum Press, New York, NY (1973)	✓
	31	Berge, S.M., et al., "Pharmaceutical Salts" <i>Journal of Pharmaceutical Sciences</i> 66:1-19 (1977)	✓
	32	Chitaley, K., et al., "Antagonism of Rho-Kinase Stimulates Rate Penile Erection via a Nitric Oxide-Independent Pathway" <i>Nature Medicine</i> 7:119-122 (2002)	✓
	33	Degenhardt, T.P., et al., "Chemical Modification of Proteins by Methylglyoxal" <i>Cell Mol. Biol.</i> , 44:1139-1145 (1998)	✓
	34	Dyer, D.G., et al., "Accumulation of Maillard Reaction Products in Skin Collagen in Diabetes and Aging" <i>J. Clin. Invest.</i> , 91:2463-2469 (1993)	✓
	35	Dyer, D.G., et al., "Formation of Pentosidine during Nonenzymatic Browning of Proteins by Glucose" <i>J. Biol. Chem.</i> , 266:11654-11660 (1991)	✓
	36	Greene, T.W., "Protection for the Amino Group" <i>Protective Groups in Organic Synthesis</i> , John Wiley and Sons, New York, NY, Chapter 7 (1981)	✓
	37	Hammes, H.P., et al., "Diabetic Retinopathy Risk Correlates with Intracellular Concentrations of the Glycoxidation Product N <sup>ε</sup> -(Carboxymethyl) Lysine Independently of Glycohaemoglobin Concentrations" <i>Diabetologia</i> , 42:603-607 (1999)	✓
	38	Hoffman, M.A., et al., "RAGE Mediates a Novel Proinflammatory Axis: A Central Cell Surface Receptor for S100/Calgranulin Polypeptides" <i>Cell</i> , 97:889-901 (1999)	✓
	39	Hori, O., et al., "The Receptor for Advanced Glycation End Products (RAGE) Is a Cellular Binding site for Amphoterin" <i>J. Biol. Chem.</i> , 270:25752-761 (1995)	✓
	40	Huttunen, H.J., et al., "Receptor for Advanced Glycation End Products (RAGE)-Mediated Neurite Outgrowth and Activation of NF-Kappa B Require the Cytoplasmic Domain of the Receptor But Different Downstream Signaling Pathways" <i>J. Biol. Chem.</i> 274(28):19919-24 (1999)	✓

Please type a plus sign (+) inside this box

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

PTO/SB/O&A (08-00)  
Approved for use through 10/31/2002. OMB 0651-0031  
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Substitute for form 1449APTO

# INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 3 of 4

Complete if Known

Application Number 10/091,759  
Filing Date March 5, 2002  
First Named Inventor Adnan M.M. Mjalli  
Group Art Unit 1614  
Examiner Name Unassigned  
Attorney Docket Number 41305-271123 (2001-)  
Express Mail Certificate EV 032 196 842 US

RECEIVED

AUG 05 2002

TECH CENTER 1600/2900

41	Kumar, S.R., et al., "RAGE at the Blood-Brain Barrier Mediates Neurovascular Dysfunction Caused by Amyloid $\beta_{1-40}$ Peptide" <i>Neurosci. Program</i> , 141-#255.19 (2000)	✓
42	Leder, A. et al., "v-HA-ras Transgene Abrogates the Initiation Step in Mouse Skin Tumorigenesis: Effects of Phorbol Esters and Retinoic Acid" <i>Proc. Natl. Acad. Sci., USA</i> , 87:9178-9182 (1990)	✓
43	Li, J. et al., "Sp1-Binding elements in the Promoter of RAG Are Essential for Amphoterin-Mediated Gene Expression in Cultured Neuroblastoma Cells." <i>J. Biol. Chem.</i> , 273:30870-30878 (1998)	✓
44	Li, J. et al., "Characterization and Functional Analysis of the Promoter of RAGE, the Receptor for Advanced Glycation End Products," <i>J. Biol. Chem.</i> , 272:16498-16506 (1997)	✓
45	Lugering, N. et al., "The Myeloid Related Protein MRP8/14 (27E10 Antigen)—Usefulness as a Potential Marker for Disease Activity in Ulcerative Colitis and Putative Biological Function" <i>Eur. J. Clin. Invest.</i> , 25:659-664 (1995)	✓
46	Miyata, T. et al., " $\beta_2$ -Microglobulin Modified with Advanced Glycation End Products Is a Major Component of Hemodialysis-Associated Amyloidosis" <i>J. Clin. Invest.</i> , 92:1243-1252 (1993)	✓
47	Miyata, T. et al., "The Receptor for Advanced Glycation End Products (RAGE) Is a Central Mediator of the Interaction of AGE- $\beta_2$ Microglobulin with Human Mononuclear Phagocytes Via an Oxidant-Sensitive Pathway" <i>J. Clin. Invest.</i> , 98:1088-1094 (1996)	✓
48	Neeper, M., et al., "Cloning and Expression of a Cell Surface Receptor for Advanced Glycosylation End Products of Proteins" <i>J. Biol. Chem.</i> , 267:14998-15004 (1992)	✓
49	Parkkinen, J. et al., "Amphoterin, the 30-kDa Protein in a Family of HMG1-Type Polypeptides" <i>J. Biol. Chem.</i> , 268:19726-19738 (1993)	✓
50	Rammes, A. et al., "Myeloid-Related Protein (MRP) 8 and MRP 14, Calcium-Binding Proteins of the S100 Family, Are Secreted by Activated Monocytes via a Novel, Tubulin-Dependent Pathway" <i>J. Biol. Chem.</i> , 272:9496-9502 (1997)	✓
51	Rauvala, H. et al., "Isolation and Some Characteristics of an Adhesive Factor of Brain That Enhances Neurite Outgrowth in Central Neurons" <i>J. Biol. Chem.</i> , 262:16625-16635 (1987)	✓
52	Reddy, S. et al., "N <sup>ε</sup> -(Carboxymethyl) Lysine Is a Dominant Advanced Glycation End Product (AGE) Antigen in Tissue Proteins" <i>Biochem.</i> , 34:10872-10878 (1995)	✓
53	Schafer, B.W., et al., "The S100 Family of EF-Hand Calcium-Binding Proteins: Functions and Pathology" <i>TIBS</i> , 21:134-140 (1996)	✓
54	Schleicher, E.D., et al., "Increased Accumulation of the Glycoxidation Product N <sup>ε</sup> -(Carboxymethyl) Lysine in Human Tissues in Diabetes and Aging" <i>J. Clin. Invest.</i> , 99(3):457-468 (1997)	✓
55	Schmidt, A.M. et al., "The Dark Side of Glucose" <i>Nature Med.</i> , 1:1002-1004 (1995)	✓

Please type a plus sign (+) inside this box

PTO/SB/08A (08-00)

Approved for use through 10/31/2002. OMB 0651-0031  
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449APTO

# INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 4 of 4

Complete if Known

Application Number	10/091,759
Filing Date	March 5, 2002
First Named Inventor	Adnan M.M. Mjalli
Group Art Unit	1614
Examiner Name	Unassigned
Attorney Docket Number	41305-271123 (2001-21)
Express Mail Certificate	EV 032 196 842 US

RECEIVED

AUG 05 2002

TECH CENTER 1600/2900

56	Schmidt, A.M., et al., "The V-Domain of Receptor for Advanced Glycation Endproducts (RAGE) Mediates Binding of AGEs: A Novel Target for Therapy of Diabetic Complications." <i>Supplement to Circulation</i> Vol. 96, #194 (1997)	✓
57	Taguchi, A. et al., "Blockade of RAGE—Amphoterin Signalling Suppresses Tumour Growth and Metastases" <i>Nature</i> , 405:354-360 (2000)	✓
58	Tanaka, N., et al., "The Receptor for Advanced Glycation End Products Is Induced by the Glycation Products Themselves and Tumor Necrosis Factor- $\alpha$ through Nuclear Factor- $\kappa$ B, and by 17 $\beta$ -Estradiol through Sp-1 in Human Vascular Endothelial Cells" <i>J. Biol. Chem.</i> , 275:25781-25790 (2000)	✓
59	Teillet et al., "Food Restriction Prevents Advanced Glycation End Product Accumulation and Retards Kidney Aging in Lean Rats" <i>J. Am. Soc. Nephrol.</i> , 11:1488-1497 (2000)	✓
60	Vlassara, H., "Advanced Glycation End-Products and Atherosclerosis" <i>The Finnish Medical Society DUODECIM, Ann. Med.</i> , 28:419-426 (1996)	✓
61	Wautier et al., "Receptor-Mediated Endothelial Cell Dysfunction in Diabetic Vasculopathy: Soluble Receptor for Advanced Glycation End Products Blocks Hyperpermeability in Diabetic Rats" <i>J. Clin. Invest.</i> , 97:238-243 (1996)	✓
62	Yan, S.-D., et al., "RAGE and Amyloid- $\beta$ Peptide Neurotoxicity in Alzheimer's Disease" <i>Nature</i> 382:685-691 (1996)	✓
63	Yan, S.-D., et al., "An Intracellular Protein That Binds Amyloid- $\beta$ Peptide and Mediates Neurotoxicity in Alzheimer's Disease" <i>Nature</i> , 389:689-695, (1997)	✓
64	Yan, S.-D. et al., "Amyloid- $\beta$ Peptide—Receptor for Advanced Glycation Endproduct Interaction Elicits Neuronal Expression of Macrophage-Colony Stimulating Factor: A Proinflammatory Pathway in Alzheimer Disease" <i>Proc. Natl. Acad. Sci., USA</i> , 94:5296-5301 (1997)	✓
65	Yan, S.-D. et al., "Receptor-Dependent Cell Stress and Amyloid Accumulation in Systemic Amyloidosis" <i>Nat. Med.</i> 6:643-651 (2000)	✓
66	Yan, S.-D. et al., "Enhanced Cellular Oxidant Stress by the Interaction of Advanced Glycation Endproducts With Their Receptors Binding Proteins" <i>J. Biol. Chem.</i> 269:9889-9897 (1994)	✓
67	Zimmer, D. et al., The S100 Protein Family: History, Function, and Expression" <i>Brain Res. Bull.</i> , 37:417-429 (1995)	✓
68	International Search Report for PCT/US 01/17251 dated 8/14/01	✓
Examiner Signature		Date Considered

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number. <sup>2</sup> Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231.

DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

41305-271123

WINLIB01:956774.1